



Patent  
45198.00027.RCE2(CON1)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Erion *et al.*

Serial No.: 09/978,454

Filed: October 15, 2001

Title: **NOVEL PRODRUGS FOR  
PHOSPHORUS-CONTAINING  
COMPOUNDS**

Group Art Unit: 1616

Examiner: Dameron Jones

**INFORMATION DISCLOSURE STATEMENT UNDER 37 CFR § 1.97(b)(3)**

Mail Stop RCE  
Commissioner for Patents  
P. O. Box 1450  
Alexandria, VA 22313-1450

Sir:

In compliance with the Applicant's duty under 37 CFR § 1.56, the following information is brought to the attention of the Examiner. The items are listed on the attached form PTO-1449 and copies are enclosed for the convenience of the Examiner.

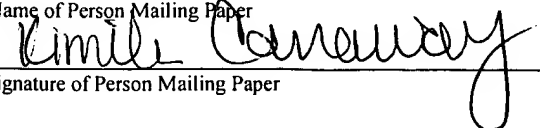
The items identified in this Information Disclosure Statement (IDS) may or may not be "material" pursuant to 37 CFR § 1.56 and the submission thereof by Applicant shall not be construed as an admission that any such patent, publication or other information referred to therein is material

CERTIFICATE OF MAILING  
(37 C.F.R. § 1.8a)

I hereby certify that this paper (along with anything referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as First Class Mail in an envelope addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

January 30, 2004  
Date of Deposit

SAN/81741.1

Kimila Carraway  
Name of Person Mailing Paper  
  
Signature of Person Mailing Paper

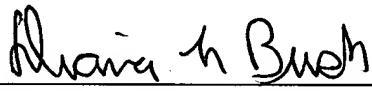
or considered to be material (37 CFR § 1.97(h)), or even qualifies as "prior art" under 35 USC § 102 with respect to this invention unless specifically designated by Applicant as such.

The filing of this IDS shall not be construed to mean that a search has been made or that no other material information, as defined in 37 CFR § 1.56, exists.

The attached IDS is being filed in accordance with 37 CFR §§ 1.97 and 1.98. This IDS is believed to be timely in that it is being submitted under 37 CFR § 1.97(b)(3), that is before the mailing of a first Office Action on the merits. Thus, no petition or fee is required. However, if the undersigned representative of Applicant is in error in this regard, then the Examiner is requested to consider this IDS as filed under § 1.97(c) and is further authorized to charge any fee required by the filing of these papers to Paul, Hastings, Janofsky & Walker's Deposit Account No. **50-2613**.

Respectfully submitted,

Dated: 1/30/04

By:   
Diana L. Bush, Esq., Ph.D.  
Reg. No. 51,109

**PAUL, HASTINGS, JANOFSKY & WALKER LLP**  
3579 Valley Centre Drive  
San Diego, CA 92130-2081  
Phone: (858) 720-2500  
Fax: (858) 720-2555

Please type a plus sign (+) inside this box → +

PTO/SB/08A (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449A/PTO

## INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 1 of 3

### Complete if Known

Application Number 09/978,454  
Filing Date October 15, 2001  
First Named Inventor Erion et al.  
Group Art Unit 1616  
Examiner Name Dameron Jones  
Attorney Docket Number 032465.00027.RCE2(CON1)

### U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code <sup>2</sup> (if known)			
	AA	6,054,587	1	Reddy et al.	04/25/00	
	AB	6,110,903	1	Kasibhatla et al.	08/29/00	
	AC	6,284,748	1	Dang et al.	09/04/01	
	AD	6,294,672	1	Reddy et al.	09/25/01	
	AF	6,399,782	1	Kasibhatla et al.	06/04/02	
	AE	6,489,476	1	Dang et al.	12/03/02	

### FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
		Office <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)				

### NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
		Beaucage and Iyer, "The Synthesis of Modified Oligonucleotides by the Phosphoramidite Approach and Their Applications," <u>Tetrahedron</u> , 49(28):6123-6194 (1993).	
		Borch and Millard, "The Mechanism of Activation of 4-Hydroxycyclophosphamide," <u>J. Med. Chem.</u> , 30:427-431 (1987).	
		Cooper et al., "Use of Carbohydrate Derivatives for Studies of Phosphorus Stereo-chemistry. Part II. Synthesis and Configurational Assignments of 1,3,2-Oxathiaphosphorinan-2-ones and 1,3,2-Dioxaphosphorinan-2-thiones," <u>J.C.S. Perkin I</u> , 3/2422:1049-1052 (1973).	
		Clercq et al., "A Novel Selective Broad-spectrum Anti-DNA Virus Agent," <u>Nature</u> , 323:464-467 (1986).	

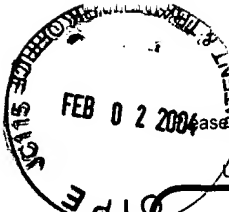
Examiner  
Signature

Date  
Considered

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation is not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number. <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.



Type a plus sign (+) inside this box → +

PTO/SB/08A (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)		<b>Substitute for form 1449A/PTO</b>	
		<b>Complete if Known</b>	
		Application Number	09/978,454
		Filing Date	October 15, 2001
		First Named Inventor	Erion et al.
		Group Art Unit	1616
Examiner Name	Dameron Jones		
Attorney Docket Number	032465.00027.RCE2(CON1)		
Sheet	2	of	3

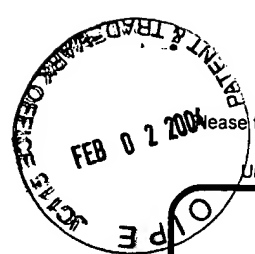
NON PATENT LITERATURE DOCUMENTS			
Examiner Initials <sup>1</sup>	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
		Farquhar et al., "Synthesis and Antitumor Evaluation of Bis[(pivaloyloxy)methyl] 2'-Deoxy-5-fluorouridine 5'-Monophosphate (FdUMP): A Strategy to Introduce Nucleotides into Cells," <u>J. Med. Chem.</u> , 37:3902-3909 (1994).	
		Friis and Bundgaard, "Prodrugs of Phosphates and Phosphonates: Novel Lipophilic $\alpha$ -acyloxyalkyl Ester Derivatives of Phosphate- or Phosphonate Containing Drugs Masking the Negative Charges of these Groups," <u>Euro. J. Pharm. Sci.</u> , 4:49-59 (1996).	
		Harada et al., "Resolution of 1,3-alkanediols Via Chiral Spiroketal Derived from <i>l</i> -Menthone," <u>Tetrahedron</u> , 28(41):4843-4846 (1987).	
		Khorana et al., "Cyclic Phosphates. III. Some General Observations on the Formation and Properties of Five-, Six- and Seven-membered Cyclic Phosphate Esters," <u>Brit. Col. Res. Couns.</u> , 79:430-436 (1957).	
		Korba et al., "Liver-targeted Antiviral Nucleosides: Enhanced Antiviral Activity of Phosphatidyl-dideoxyguanosine Versus Dideoxyguanosine in Woodchuck Hepatitis Virus Infection <i>In Vivo</i> ," <u>Hepatology</u> , 23(5):958-963 (1996).	
		Lefebvre et al., "Mononucleoside Phosphotriester Derivatives with <i>S</i> -acyl-2-thioethyl Bioreversible Phosphate-protecting Groups: Intracellular Delivery of 3'-azido-2',3'-dideoxythymidine 5'-monophosphate," <u>J. Med. Chem.</u> , 38:3941-3950 (1995).	
		Ludeman et al., "Synthesis and Antitumor Activity of Cyclophosphamide Analogues. 4. Preparation, Kinetic Studies, and Anticancer Screening of "Phenylketophosphamide" and Similar Compounds Related to the Cyclophosphamide Metabolite Aldophosphamide," <u>J. Med. Chem.</u> , 29:716-727 (1986).	
		McGuigan et al., "Intracellular Delivery of Bioactive AZT Nucleotides by Aryl Phosphate Derivatives of AZT," <u>J. Med. Chem.</u> , 36:1048-1052 (1993).	
		Mosbo and Verkade, "Dipole Moment, Nuclear Magnetic Resonance, and Infrared Studies of Phosphorus Configurations and Equilibria in 2-R-2-Oxo-1,3,2-dioxaphosphorinanes," <u>J. Org. Chem.</u> , 42(9):1549-1555 (1977).	
		Nakayama and Thompson, "A Highly Enantioselective Synthesis of Phosphate Triesters," <u>J. Am. Chem. Soc.</u> , 112:6936-3942 (1990).	

Examiner Signature	Date Considered
--------------------	-----------------

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation is not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number. <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.



Please type a plus sign (+) inside this box → +

PTO/SB/08A (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449A/PTO		<b>Complete if Known</b>	
		<b>Application Number</b>	09/978,454
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)		<b>Filing Date</b>	October 15, 2001
		<b>First Named Inventor</b>	Erion et al.
		<b>Group Art Unit</b>	1616
		<b>Examiner Name</b>	Dameron Jones
		<b>Attorney Docket Number</b>	032465.00027.RCE2(CON1)
Sheet	3	of	3

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
		Ramachandran et al., "Efficient General Synthesis of 1,2- and 1,3-diols in High Enantiomeric Excess via the Intramolecular Asymmetric Reduction of the Corresponding Ketoalkyl Diisopinocampheylborinate Intermediates," <u>Tetrahedron</u> , 38(5):761-764 (1997).	
		Starrett, Jr. et al., "Synthesis, Oral Bioavailability Determination, and <i>in Vitro</i> Evaluation of Prodrugs of the Antiviral Agent 9-[2-(Phosphonomethoxy)ethyl]adenine (PMEA)," <u>J. Med. Chem.</u> , 37:1857-1864 (1994).	
		Thompson et al., "Synthesis, Bioactivation and Anti-HIV Activity of the Bis(4-acyloxybenzyl) and Mono(4-acyloxybenzyl) Esters of the 5'-monophosphate of AZT," <u>J. Chem. Soc.</u> , 2/06723D:1239-1245 (1993).	
		Weber and Waxman, "Activation of the Anti-cancer Drug Ifosfamide by Rat Liver Microsomal P450 Enzymes," <u>Biochem. Pharm.</u> , 45(8):1685-1694 (1993).	
		Zon et al., "NMR Spectroscopic Studies of Intermediary Metabolites of Cyclophosphamide. A Comprehensive Kinetic Analysis of the Interconversion of <i>cis</i> - and <i>trans</i> -4-Hydroxycyclophosphamide with Aldophosphamide and Concomitant Partitioning of Aldophosphamide Between Irreversible Fragmentation and Reversible Conjugation Pathways," <u>J. Med. Chem.</u> 27:466-485 (1984).	

Examiner Signature	Date Considered
--------------------	-----------------

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation is not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number. <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.